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Effect of Trichloroethylene on the Exploratory and Locomotor Activity of Rats Exposed during Development

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EFFECT OF TRICHLOROETHYLENE ON THE EXPLORATORY AND LOCOMOTOR ACTIVITY OF RATS EXPOSED DURING DEVELOPMENT

by

Douglas H. Taylor[1], Kirk E. Lagory[1], Daniel J. Zaccaro[1], Ronald J. Pfohl[1] and R. Dana Laurie[2]

[1]Department of Zoology, Miami University, Oxford, Ohio 45056

[2]Toxicology and Microbiology Division, U.S. Environmental Protection Agency, Cincinnati, Ohio 45268

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Project Officer

R. Dana Laurie
Toxicology and Microbiology Division
U.S. Environmental Protection Agency
Cincinnati, Ohio 45268

HEALTH EFFECTS RESEARCH LABORATORY
OFFICE OF RESEARCH AND DEVELOPMENT
U.S. ENVIRONMENTAL PROTECTION AGENCY
RESEARCH TRIANGLE PARK, NORTH CAROLINA 27711

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DOUGLAS H. TAYLOR, KIRK E. LAGORY, DANIEL J. ZACCARO, RONALD J. PFOHL and R. DANA LAURIE. Department of Zoology, Miami University, Oxford, Ohio 45056 and Health Effects Research Laboratory, USEPA, Cincinnati, Ohio 45268 USA

ABSTRACT

Trichloroethylene (TCE) is a common contaminant of underground water supplies. To examine the effect of TCE on the developing central nervous system, rats were exposed to TCE throughout gestation until 21 days postpartum via their dams' drinking water. TCE concentrations of 312 ppm, 625 ppm and 1250 ppm were tested. Exploratory behavior was higher in 60- and 90-day old male rats which were exposed to any level of TCE. The effect of TCE-exposure on locomotor activity (running wheel) was also examined in 60-day old males (625 and 1250 ppm exposure groups). Locomotor activity was significantly higher in rats exposed to 1250 ppm TCE. These data suggest that TCE has long-term effects on behavior.

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INTRODUCTION

Trichloroethylene (TCE) is an unsaturated chlorinated hydrocarbon which is commonly used as an industrial solvent (ref.1). Historically, the most common route of TCE-intake by humans was via inhalation. Consequently, most research has focused on the effects of TCE vapors on physiological and behavioral processes and relatively little attention has been paid to the effects of TCE exposure via drinking water. However, it is now well established that TCE is a common drinking water contaminant (ref.2, 3, 4, 5, 6).

TCE and its metabolites (e.g., trichloroethanol and trichloroacetic acid) are neurotoxic and affect many parts of the brain (ref.7, 8, 9, 10). The neurotoxic qualities of TCE are presumably the result of its effects on the lipid structure of nerve cell membranes (ref.11) and its concomitant impairment of membrane permeability (ref.12). TCE may hinder mobilization of action potentials (ref.13).

We chose to examine the effects of TCE in rats exposed during development for a variety of reasons. The fetus and neonate are particularly susceptible to toxic insult due to their reduced ability to detoxify compounds. In addition, toxicants can have more serious, irreversible consequences if developmental processes are altered. TCE easily crosses the placenta and is found in fetal blood shortly after maternal exposure (ref.14). Despite this, few studies have investigated the effects of prenatal and early postnatal exposure to TCE on behavior.

In our study, rat pups were exposed via their dam's drinking water during gestation and lactation, the period of the most active CNS development (ref. 14). Here we report that prenatal and postnatal exposure (to 21 days of age) to TCE at concentrations of 312 ppm, 625 ppm, and 1250 ppm results in increased exploratory activity in 60 and 90 day old rats. Locomotor activity (wheel running) was higher in rats exposed to 1250 ppm TCE at 60 days of age.

METHODS

Female Sprague-Dawley rats were exposed to TCE at several nominal concentrations (312, 625, and 1250 mg/l) in their drinking water. TCE was dissolved in distilled water without the use of a vehicle to avoid the possible confounding effects of the vehicle. Drinking water was provided ad libitum and was changed every 3 days. The degradation of TCE in the water bottles was determined using a gas chromatograph (Hewlett-Packard Model 5792) to estimate the dosage received by the dams. Experimental dams received TCE from 14 days prior to breeding, through gestation, until the pups were weaned at 21 days of age; control dams received distilled water. Thus, experimental pups were indirectly exposed prenatally and postnatally to TCE, or its byproducts. Litters were culled at birth to eight pups. Male rats derived from experimental and control dams were used as the subjects in this study.

Exploratory behavior during a 15-min. sampling period was measured in an apparatus similar to that described by Barlyne (ref.15; Fig. 1a). Individual rats were tested once at either 28, 60, or 90 days of age.

A residential cage apparatus (Fig. 1b) was used to monitor wheel-running, feeding, and drinking behavior in rats for 24 hr/day from 55-60 days of age. Rats were allowed to acclimate to the residential cage for 4 days prior to the onset of data collection.

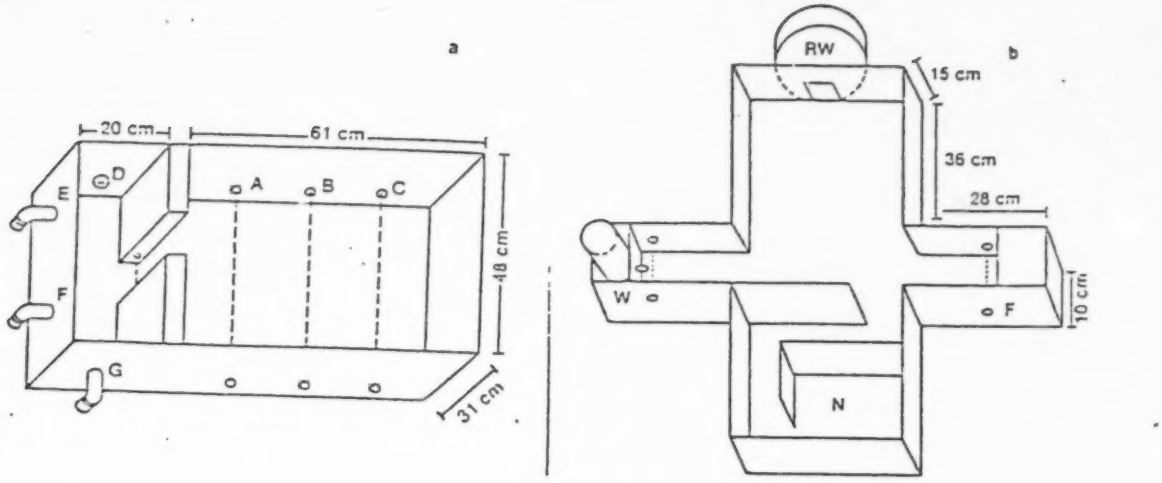

Fig. 1 (a). Exploratory apparatus. The apparatus consisted of 2 chambers: an arena crossed by 3 infrared beams (A-C) and an alcove with 4 exploratory ports bisected by infrared beams (D-G). Cups at the end of these ports contained used bedding from an adult male rat to provide an olfactory stimulus for exploration. A subject explored these ports by inserting its head into the opening. (b). Residential cage. Infrared beams were positioned to monitor feeding (F) and drinking (W) behavior; wheel revolutions (RW) were registered electromagnetically. A nest area (N) was provided. Data from both apparatuses were recorded by a Hewlett-Packard 9825A desktop computer.

Statistical analyses were performed using the Statistical Analysis System (ref.16). One-factor analyses of variance were used to test for treatment effects on the frequency of exploration and the number of beams crossed in the arena at 28, 60, and 90 days of age. Three-factor analyses of variance were used to analyze for treatment, time, and day effects on wheel-running, feeding and drinking in the residential cage. Only the dark part of the photoperiod was analyzed because rats were essentially inactive in the residential cage when the lights were on. Dark hours were pooled into 3-hr periods for analysis to account for ultradian rhythms in rat activity (ref.17). Probability values ≤ 0.05 were considered significant.

RESULTS

Total consumption of TCE during the experiment was calculated from mean water consumption values and the mean concentration of TCE in the drinking water of treated rats. Total consumption values were: 312 ppm - 646 mg, 625 ppm - 1102 mg, 1250 ppm - 1991 mg.

At 28 days of age, no difference in the level of exploratory activity was seen among treatment groups ($P = 0.70$). However, at 60 and 90 days of age, rats exposed to TCE exhibited increased levels of exploration (see Fig. 2a and

2b). No treatment effects were detected at any age on the number of beams crossed in the arena (28 days: P = 0.68; 60 days: P = 0.24; 90 days: P = 0.29).

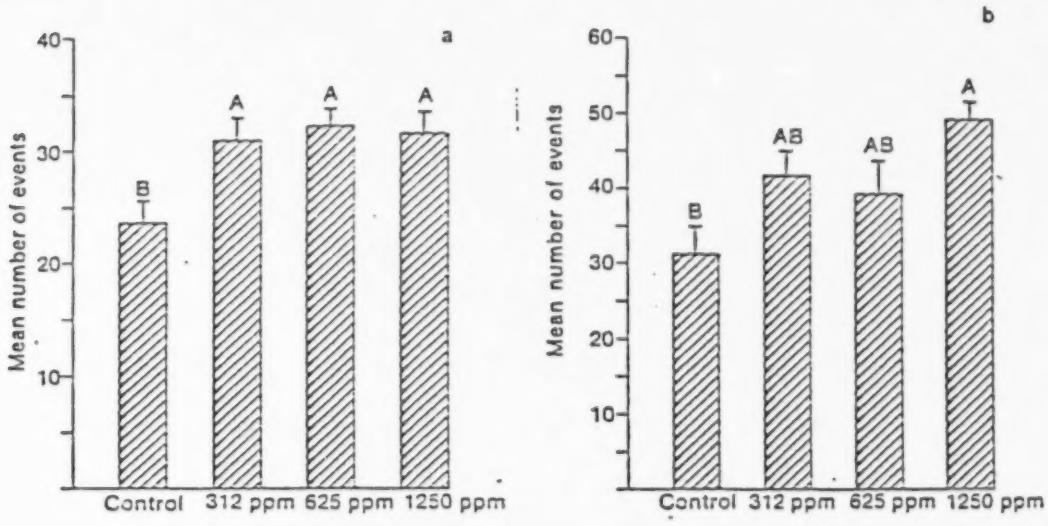

Fig. 2. Mean number of exploratory events in 60- (a) and 90- (b) day old rats (+ 2 SE's). Means with the same letter are not significantly different. Treatment effect at 60 days: F = 2.97, P = 0.03; at 90 days: F = 4.7, P = 0.01.

From 55-60 days of age, rats exposed to 1250 ppm TCE were more active on the wheel in the residential cage than were controls or those exposed to 625 ppm TCE (see Fig. 3). This difference among treatment groups was especially pronounced during the initial 3 hours of darkness when rats at this age were most active (dose * time interaction: P = 0.001). No significant differences were detected among treatment groups for the levels or timing of feeding and drinking activities during the night (P > 0.05).

DISCUSSION

Our data suggest that exposure to TCE during the period of active CNS development can lead to behavioral changes which are present at least 2 months after cessation of exposure. Exploratory behavior appeared to be more sensitive than locomotor behavior (wheel-running) to the effects of TCE. This is indicated by the increased levels of exploratory activity in rats exposed to any concentration of TCE $\geq$ 312 ppm; in contrast, wheel-running was altered only in rats exposed to 1250 ppm TCE.

Other investigators have reported either increased activity or exploratory behavior (ref.18, 19, 20) possibly as a result of reduction of fear or inhibition. Battig et al. (ref. 21) found that adult rats subjected to long-term exposure to TCE vapors (360-420 ppm for 8 hrs/day, 5 days/week for 44 weeks) exhibited increased levels of exploration relative to controls when tested

during the 43rd and 44th week. Exploratory tests performed 5 to 6 days after cessation of exposure, however, indicated no differences between controls and treated animals. These data indicate that the behavioral changes following TCE exposure are reversible if exposure occurs during adulthood.

Behavioral changes after exposure to TCE are presumably linked to the CNS dysfunction documented in animals exposed to TCE. The differences between control and TCE-exposed rats observed in our study long after the termination of exposure indicates that TCE-mediated damage to the CNS during development may be permanent.

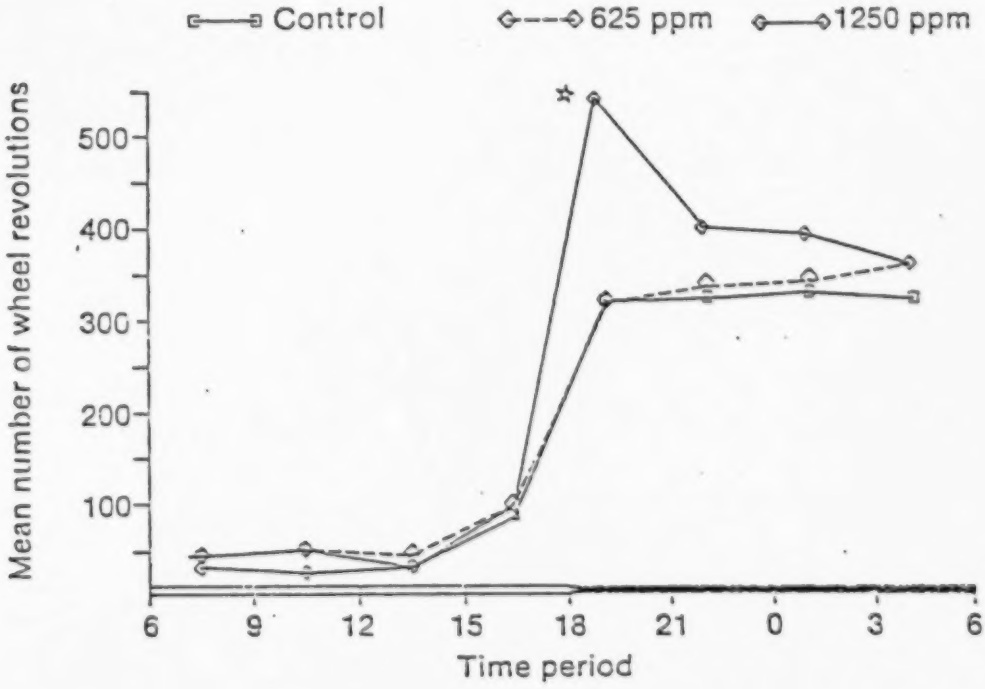

Fig. 3. Wheel-running in the residential cage. Rats exposed to 1250 ppm TCE were more active during the initial period of darkness (*) than were controls or rats exposed to 625 ppm.

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